Molecular Physiology Laboratory（2021）
Chief Scientist: Rikiya Watanabe (Ph.D.)

(0) Research field
CPR Subcommittee**:** Biology

Keywords: membrane protein, artificial cell membrane, artificial cell, bioMEMS, digital biology

(1) Long-term goal of laboratory and research background

Our study aims to understand cellular functions using a bottom-up approach from the single molecule level. To achieve this, we are attempting to elucidate the mechanism by which individual biomolecules or their networks function in a precise manner, by developing novel single-molecule techniques using multidisciplinary approaches, including biophysics, bioMEMS, and chemical biology. In addition, we are developing a methodology to investigate correlations between genetic mutations, dysfunctions, and diseases with single molecule sensitivity, which would provide new insights for biological as well as pharmaceutical studies.

(2) Current research activities (FY2021)

Development of automated platform for rapid and sensitive COVID-19 diagnosis

In the ongoing COVID-19 pandemic, there is an urgent need to establish a versatile diagnostic method for viral infections. The PCR and antigen tests are widely used for the diagnosis of viral infections; however, these methods generally have technical drawbacks in terms of sensitivity, accuracy, and throughput, making it difficult to efficiently analyze a large volume of specimens with high sensitivity and accuracy. To address these issues, we have successfully developed an innovative technology using CRISPR-Cas13a (SATORI method)[1] that can detect viral RNA from SARS-CoV-2 at single molecule level with high sensitivity and throughput (the fastest in the world) (Fig. 1). The SATORI method was useful for rapid and sensitive diagnosis of COVID-19; however, full automation of the diagnostic process was essential for its implementation in society.

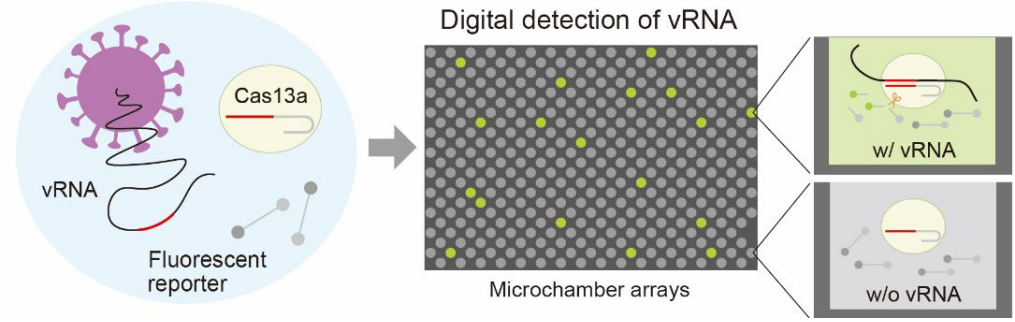

Fig. 1 Amplification-free rapid detection platform of viral RNA (SATORI method)

Last fiscal year (FY2021), we developed an automated platform on SATORI (opn-SATORI) [2] for fully automated diagnosis of viral infections using the SATORI method by incorporating the custom-made dispensing robot (Fig. 2). Using clinical specimens of COVID-19, we demonstrated that opn-SATORI can detect viral RNA from SARS-CoV-2 with high sensitivity (1.4 copies/μL) comparable to that of PCR, and discriminate between SARS-CoV-2 variants of concern in ~ 9 min with an accuracy of 98%. In addition, by developing plastic microchips and optimizing assay reagents, we have succeeded in reducing the cost of opn-SATORI to less than $2 per test, making it ideal for social implementation.

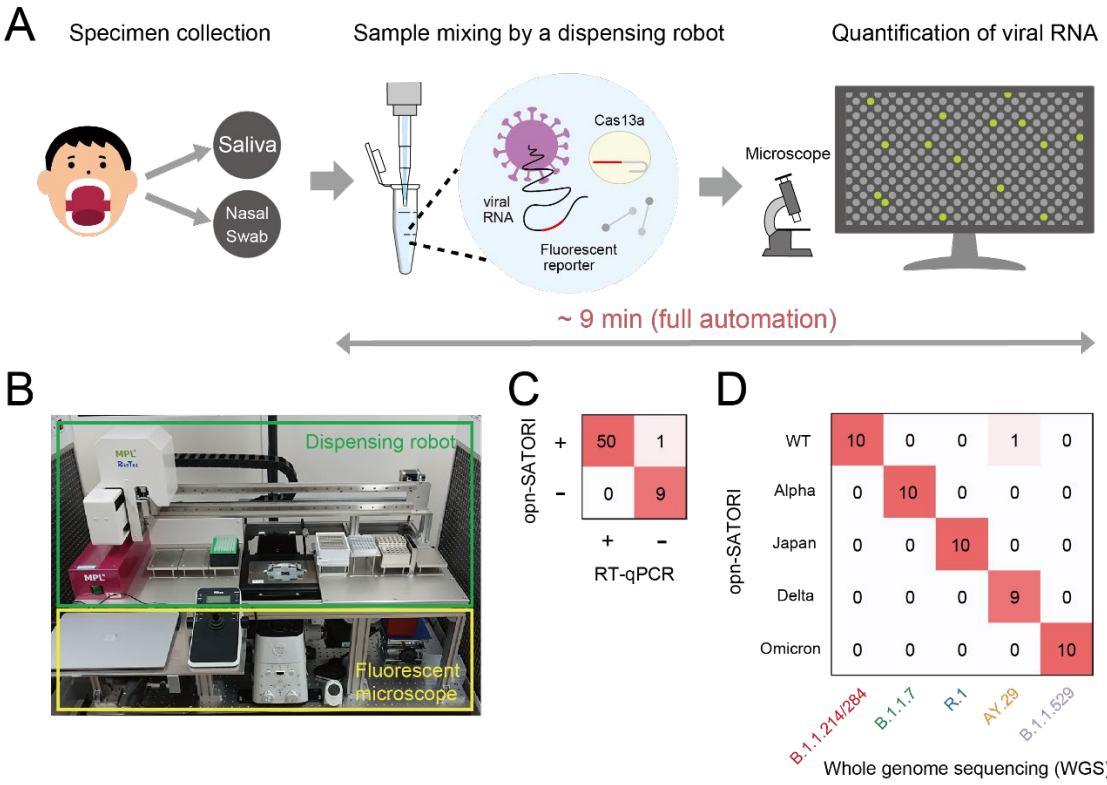

Fig. 2 Automated platform on SATORI (opn-SATORI) for COVID-19 diagnosis
(A) Schematics of COVID-19 diagnosis, (B) Overall view, (C, D) Comparison of opn-SATORI and PCR/WGS results in SARS-CoV-2 detection and variant discrimination.

We demonstrated that opn-SATORI is a sensitive, rapid, and automated platform for viral RNA detection that can precisely diagnose SARS-CoV-2 and its variants. Given that CRISPR-Cas13a-based methods have been used to detect RNA biomarkers for cancer diagnosis, opn-SATORI may serve as a versatile platform for diverse applications, including diagnosis of viral infections and evaluation of disease-related biomarkers for liquid biopsy (Fig. 3). We believe that opn-SATORI will be a key technology for high-throughput genetic diagnostics.

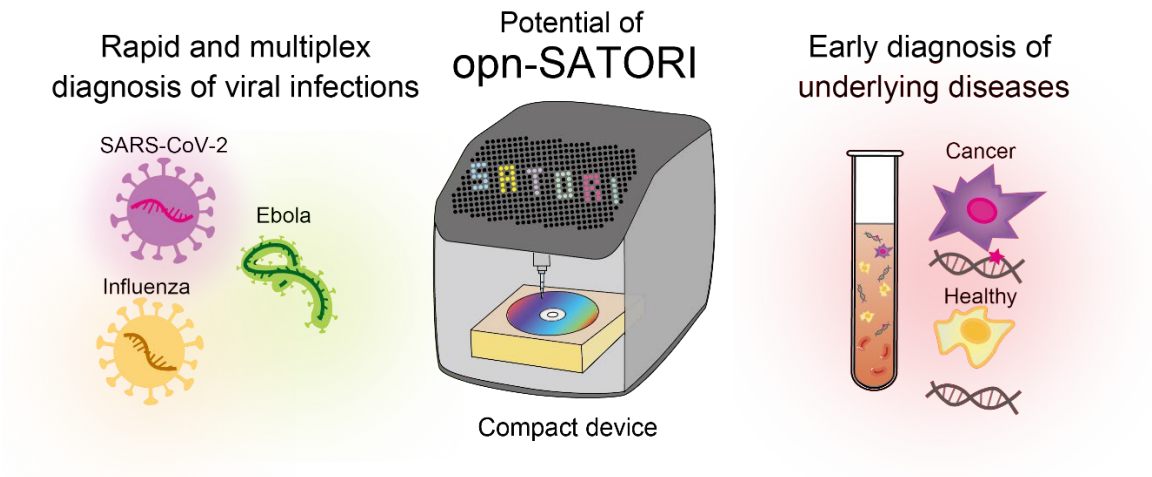

Fig. 3 Potential of opn-SATORI for liquid biopsy

(3) Members

(Chief Scientist)
Rikiya Watanabe
(Research Scientist)
Jun Ando, Hajime Shinoda
(Special Postdoctoral Researcher)
Yoshiaki Kinoshita

(Technical Staff)
Asami Makino, Chiharu Takahashi,
Tatsuya Iida, Mami Yoshimura

(4) Representative research achievements

1. "Amplification-free RNA detection with CRISPR-Cas13", Shinoda, H., Taguchi, Y., Nakagawa, R., Makino, A., Okazaki, S., Nakano, M., Muramoto, Y., Takahashi, C., Takahashi, I., Ando, J., Noda, T., *Nureki, O., *Nishimasu, H., & *Watanabe, R., ***Commun. Biol.***, 4, 476 (2021)

2. "Automated amplification-free digital RNA detection platform for rapid and sensitive SARS-CoV-2 diagnosis", Shinoda, H., Iida, T., Makino, A., Yoshimura, M., Ishikawa, J., Ando, J., Murai, K., Sugiyama, K., Muramoto, Y., Nakano, M., Kiga, K., Cui, L., Nureki, O., Takaeuchi, H., Noda, T., *Nishimasu, H., & *Watanabe, R., ***Commun. Biol.***, 5, 473 (2022)

Laboratory Homepage
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